

REMARKS

Claims 1 to 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koketsu et al. (The Journal of Food Science, 1993, Vol. 58, No.4, pp. 743-747) ("Koketsu") and Inazu et al. (Peptide Science 1998, M. Kondo Edition, P. 153-156) ("Inazu") and in view of Yamamoto, K. (Journal of Bioscience and Bioengineering, 2001, Vol. 92, No. 6, pp. 493-501) ("Yamamoto").

The Office has identified the application as claiming: a process for preparing asparagine-linked oligosaccharide derivatives including the steps of: (a) treating a delipidated egg yolk with a protease, (b) treating with a peptidase to obtain a mixture of asparagine-linked oligosaccharides, (c) introducing a lipophilic protective group into the asparagine-linked oligosaccharides, and (d) subjecting the mixture of asparagine-linked oligosaccharide derivatives to a fractionating chromatography using a reverse phase column to separate the mixture (claim 1); delipidating an avian egg yolk with an organic solvent (claim 2); [the asparagine-linked oligosaccharide derivatives are] penta- (hepta-, nona-) to undecasaccharide derivatives (claims 3-6); the lipophilic protective group is a carbonate-containing group (claims 7 and 8); the lipophilic protective group is Fmoc group (claims 9 and 10); the asparagine-linked oligosaccharides obtained by step (b) are

hydrolyzed before the subsequent step to cut off some sugar moieties (claim 11), and the asparagine-linked oligosaccharides obtained in the mixture by step (c) are hydrolyzed before the subsequent step to cut off some sugar moieties (claim 12).

The Office identifies Koketsu as teaching a process for preparing asparagine-linked oligosaccharide derivatives, treating an avian egg yolk with ethanol (organic solvent) to obtain delipidated egg yolk (DEY), and separating the mixture of oligosaccharides by reverse-phase column, the oligosaccharide derivatives are hydrolyzed to cut off some sugar moieties, and [as teaching] an undecasaccharide derivative citing p. 743, Abstract, and 2<sup>nd</sup> column, 3<sup>rd</sup> paragraph, lines 1-2; p. 744, 2<sup>nd</sup> column, 4<sup>th</sup> paragraph, lines 1-5; and p. 746, Figure 5, 3<sup>rd</sup> oligosaccharide derivative.

Inazu is cited as teaching a process for preparing asparagine-linked oligosaccharide derivatives, treating an egg with a protease (Pronase), introducing a lipophilic protective group into the asparagine-linked oligosaccharides, and subjecting the mixture of asparagine-linked oligosaccharide derivatives to a fractionating chromatography using a reverse phase column to separate the mixture, and [as teaching] penta- to undecasaccharide derivatives, citing p. 153, Abstract and p. 154, figure 1.

Yamamoto is cited as teaching that oligosaccharide moieties of some glycoconjugates have been shown to play important roles in biological phenomena such as cellular recognition, lectin binding, and viral infection, among others and as teaching the importance of synthesizing new oligosaccharide with additional functions by modification of naturally occurring oligosaccharides.

The Office's position is that a person of ordinary skill in the art, in view of the teaching of Yamamoto of the importance of synthesizing new oligosaccharides with additional functions by modification of naturally occurring oligosaccharides, and of the addition of an oligosaccharide to a substance to give it a useful function, would have been motivated to combine the teachings of Inazu and Koketsu and use delipidated egg yolk to provide a process for preparing asparagine-linked oligosaccharide derivatives.

Applicant respectfully submits that the Office has not properly supported a case of prima facie obviousness of claims 1-12 under 35 U.S.C. § 103(a).

First, the Office has not shown a proper motive to make the specific modification to the art that he has proposed. A general desire of a person of ordinary skill in the art to synthesize new oligosaccharides with additional functions by modification of naturally occurring oligosaccharides, and to add an oligosaccharide

to a substance to give it a useful function, that is allegedly taught by Yamamoto, does not provide a motive to make any specific modification to the prior art.

Second, the Office has not shown or explained why the proposed modification to the prior art would be reasonably expected to provide good results. To support a case of obviousness, the Office must show that a person of ordinary skill in the art would have had a reason to carry out the claimed process, and would have had a reasonable expectation of success in doing so.

Third, the modification proposed by the Office will not result in the claimed process. The Office's position is that it would have been obvious to substitute delipidated egg yolk of Koketsu for the egg used in the process of Inazu and that the resultant process would be the process claimed in the present application. If further modifications to the prior art are required to obtain the process of the present invention, the Office's position is not correct.

In the present invention, it is essential (a) to use a delipidated egg yolk and (b) to use a combination of a protease and a peptidase.

Koketsu discloses on page 743 and the abstract that delipidated egg yolk (DEY) was homogenized and centrifuged. The

supernatant was dialyzed by ultrafiltration using a molecular weight cut-off of 1,000. The asparagine-linked oligosaccharides in the concentrate were liberated from protein by hydrazinolysis and labeled with UV-absorbing p-amionbenzoic ethyl ester (ABEE). The ABEE-derivatized oligosaccharides were fractionated by anion exchange and reverse-phase HPLC.

In Koketsu, neither a protease nor a peptidase is used, and the product is an ABEE-derivatized oligosaccharides and not a Fmoc oligosaccharide derivative.

Inazu shows in Fig. 1, an egg treated by a protease (Pronase). However, Inazu does not use a delipidated egg yolk, and only uses a protease and not a protease and a peptidase.

Yamamoto adds nothing to the teachings of Koketsu and Inatsu.

For these reasons, the 35 U.S.C. 103(a) rejection of claims 1 to 12 is improper and removal of the rejection is in order.

However, even if it is assumed arguendo that the Office has properly supported a case of prima facie obviousness, the process of the present invention exhibits unexpectedly improved results sufficient to rebut obviousness. In support of this position, submitted herewith is a Declaration under 37 C.F.R. 1.132 of Kazuhiro FUKAE.

The Declaration includes a description of Example 1 and Comparative Examples 1 and 2.

Example 1 of the Declaration is the same as Example 1 described on pages 15 to 18 of the specification of the present application. This process employed a delipidated egg yolk as a starting material and used a combination of a protease and a peptidase, and 13.3 mg of the desired product is obtained.

In Comparative Example 1 of the Declaration, the same procedure is conducted as in Example 1 except that Actinase E in the step (b) is replaced by Orientase ONS. The desired product is obtained in an amount of 4.4 mg. Here, only protease is used and peptidase is not used.

In Comparative Example 2 of the Declaration, the same procedure is conducted as in Example 1 except that Orientase ONS in the step (a) is replaced by Actinase E. The desired product is obtained in an amount of 6.7 mg. Here, only peptidase is used and protease is not used.

The present invention employs a delipidated egg yolk as a starting material and uses a combination of a protease and a peptidase, and exhibits an excellent and unexpected effect as shown from the results obtained in Example 1 as compared to the results obtained in Comparative Examples 1 and 2. The process of the

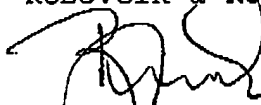
present application exhibits a two to three times increase in yield of the desired product over that Comparative Examples 1 and 2 (which also show excellent effects over the cited references).

Removal of the 35 U.S.C. 103(a) rejection of the claims is believed to be in order and is respectfully requested.

The foregoing is believed to be a complete and proper response to the Office Action dated October 5, 2007.

In the event that this paper is not considered to be timely filed, applicant hereby petitions for an appropriate extension of time. The fee for any such extension and any additional required fees may be charged to Deposit Account No. 111833.

Respectfully submitted,  
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Attachment: Declaration under 37 C.F.R. 1.132 of Kazuhiro FUKAE